CLAIMS

What is claimed is:

1. An antibody or antigen-binding fragment thereof which binds to a mammalian CC-chemokine receptor 2 or portion of said receptor, wherein said antibody or antigen-binding fragment thereof inhibits binding of a ligand to the receptor.

2. An antibody or antigen-binding fragment according to Claim 1 wherein said antibody or antigen-binding fragment thereof inhibits one or more functions associated with binding of the ligand to the receptor.

3. An antibody or antigen-binding fragment thereof according to Claim 1 wherein the mammalian CC-chemokine receptor 2 is a human CC-chemokine receptor 2.

4. An antibody or antigen-binding fragment thereof according to Claim 1 wherein the antibody or fragment thereof binds the amino-terminal domain or portion thereof of mammalian CC-chemokine receptor 2.

5. An antibody or antigen-binding fragment thereof according to Claim 4 wherein the portion of the amino-terminal domain is from about amino acid 1 to about amino acid 30.

6. An antibody or antigen-binding fragment thereof according to Claim 1 wherein the antibody is selected from the group consisting of:

a) monoclonal antibody 1D9;

b) an antibody having an epitopic specificity which is the same as or similar to that of 1D9;

c) an antibody which can compete with 1D9 for binding to mammalian CC-chemokine receptor;

d) monoclonal antibody 8G2;

e) an antibody having an epitopic specificity which is the same as or similar to that of 8G2;

f) an antibody which can compete with 8G2 for binding to mammalian CC-chemokine receptor 2; and

g) antigen-binding fragments of any one of (a) through (f) which bind to mammalian CC-chemokine receptor 2 or a portion thereof.

7. An antibody or antigen-binding fragment thereof according to Claim 1 wherein the ligand is a chemokine.

8. An antibody or antigen-binding fragment thereof according to Claim 7 wherein the chemokine is selected from the group consisting of MCP-1, MCP-2, MCP-3, MCP-4 and combinations thereof.

9. The hybridoma cell line deposited under ATCC Accession No. _____.

10. The hybridoma cell line deposited under ATCC Accession No. _____.

11. A monoclonal antibody or antigen-binding fragment thereof produced by the hybridoma cell line according to Claim 9.

12. A monoclonal antibody or antigen-binding fragment thereof produced by the hybridoma cell line according to Claim 10.

13. A test kit for use in detecting the presence of a mammalian CC-chemokine receptor 2 in a biological sample comprising

a) at least one antibody or antigen-binding fragment thereof selected from the group consisting of:
   - i) monoclonal antibody 1D9;
   - ii) an antibody having an epitopic specificity which is the same as or similar to that of 1D9;
   - iii) an antibody which can compete with 1D9 for binding to mammalian CC-chemokine receptor 2;
   - iv) monoclonal antibody 8G2;
   - v) an antibody having an epitopic specificity which is the same as or similar to that of 8G2;
   - vi) an antibody which can compete with 8G2 for binding to mammalian CC-chemokine receptor 2; and
   - vii) antigen-binding fragments of any one of (i) through (vi) which bind to mammalian CC-chemokine receptor 2 or a portion thereof; and

b) one or more ancillary reagents suitable for detecting the presence of a complex between said antibody or antigen-binding fragment thereof and said mammalian CC-chemokine receptor 2 or a portion thereof.

14. A method of inhibiting the interaction of a cell bearing mammalian CC-chemokine receptor 2 with a ligand thereof, comprising contacting said cell with an effective amount of an antibody or antigen-binding fragment thereof which binds to mammalian CC-chemokine receptor 2 or portion of said receptor and inhibits binding of said ligand to the receptor.

15. A method according to Claim 14 wherein the cell is selected from the group consisting of lymphocytes, monocytes, granulocytes, T cells, basophils, and cells comprising a recombinant nucleic acid encoding CCR2 or a portion thereof.

16. A method according to Claim 15 wherein the T cells are selected from the group consisting of CD8+ cells, CD25+ cells, CD4+ cells and CD45RO+ cells.

17. A method according to Claim 14 wherein the ligand is a chemokine.

18. A method according to Claim 17 wherein the chemokine is selected from the group consisting of MCP-1, MCP-2, MCP-3, MCP-4 and combinations thereof.

19. A method according to Claim 14 wherein the antibody or antigen-binding fragment thereof is selected from the group consisting of:

a) monoclonal antibody 1D9;

b) an antibody having an epitopic specificity which is the same as or similar to that of 1D9;

c) an antibody which can compete with 1D9 for binding to mammalian CC-chemokine receptor 2; and

d) antigen-binding fragments of any one of (a) through (c) which bind to mammalian CC-chemokine receptor 2 or a portion thereof.

20. A method of inhibiting HIV infection of a cell, comprising contacting a cell with an effective amount of a composition comprising an antibody or antigen-binding fragment thereof which binds to mammalian CC-chemokine receptor 2 or portion of said receptor and inhibits HIV entry into said cell.

21. A method according to Claim 20 wherein the cell is selected from the group consisting of lymphocytes, monocytes, macrophages, granulocytes, T cells, and cells comprising a recombinant nucleic acid encoding CCR2 or a portion thereof.

22. A method according to Claim 21 wherein the T cells are selected from the group consisting of CD8+ cells, CD25+ cells, CD4+ cells and CD45RO+ cells.

23. A method according to Claim 20 wherein the antibody or antigen-binding fragment thereof is selected from the group consisting of:

a) monoclonal antibody 1D9;

b) an antibody having an epitopic specificity which is the same as or similar to that of 1D9;

c) an antibody which can compete with 1D9 for binding to mammalian CC-chemokine receptor 2; and

d) antigen-binding fragments of any one of (a) through (c) which bind to mammalian CC-chemokine receptor 2 or a portion thereof.

24. A method of treating HIV in a patient comprising administering to the patient a composition comprising an effective amount of an antibody or antigen-binding fragment thereof which binds to mammalian CC-chemokine receptor 2 or portion of said receptor and inhibits HIV entry into said cell.

25. A method according to Claim 24 wherein the antibody or antigen-binding fragment thereof is selected from the group consisting of:

a) monoclonal antibody 1D9;
b) an antibody having an epitopic specificity which is the same as or similar to that of 1D9;
c) an antibody which can compete with 1D9 for binding to mammalian CC-chemokine receptor 2; and
d) antigen-binding fragments of any one of (a) through (c) which binds mammalian CC-chemokine receptor 2 or a portion thereof.

26. A method of detecting expression of mammalian CC-chemokine receptor 2 or portion thereof by a cell, comprising:

a) contacting a composition comprising a cell to be tested with an antibody or antigen-binding fragment thereof selected from the group consisting of:
    i) monoclonal antibody 1D9;
    ii) an antibody having an epitopic specificity which is the same as or similar to that of 1D9;
    iii) an antibody which can compete with 1D9 for binding to mammalian CC-chemokine receptor 2;
    iv) monoclonal antibody 8G2;

v) an antibody having an epitopic specificity which is the same as or similar to that of 8G2;

vi) an antibody which can compete with 8G2 for binding to mammalian CC-chemokine receptor 2;

vii) antigen-binding fragments of any one of (i) through (vi) which bind mammalian CC-chemokine receptor 2 or a portion thereof; and

viii) combinations of the foregoing, under conditions appropriate for binding of said antibody or antigen-binding fragment thereof thereto; and

b) detecting binding of said antibody or antigen-binding fragment thereof,

wherein the binding of said antibody or antigen-binding fragment thereof indicates the presence of said receptor or portion of said receptor on said cell.

27. The method of Claim 26 wherein the composition is a sample comprising human cells.

28. A method of detecting a mammalian CC-chemokine receptor 2 or portion of said receptor, comprising:

a) contacting a sample to be tested with an antibody or antigen-binding fragment thereof which is selected from the group consisting of:

i) monoclonal antibody 1D9;

ii) an antibody having an epitopic specificity which is the same as or similar to that of 1D9;

iii) an antibody which can compete with 1D9 for binding to mammalian CC-chemokine receptor 2;

iv) monoclonal antibody 8G2;

v) an antibody having an epitopic specificity which is the same as or similar to that of 8G2;

vi) an antibody which can compete with 8G2 for binding to mammalian CC-chemokine receptor 2;

vii) antigen-binding fragments of any one of (i) through (vi) which bind to mammalian CC-chemokine receptor 2 or a portion thereof; and

viii) combinations of the foregoing,

under conditions appropriate for binding of said antibody or fragment thereof thereto; and

b) detecting or measuring binding of said antibody or antigen-binding fragment thereof,

wherein the binding of said antibody or antigen-binding fragment thereof to material in said sample is indicative of the presence of a mammalian CC-chemokine receptor 2 or portion of said receptor in said sample.

29. A method according to Claim 28, wherein the sample is a cellular fraction which, in normal individuals, comprises a mammalian CC-chemokine receptor 2 or portion of said receptor.

30. A method of inhibiting a function associated with binding of a chemokine to a mammalian CC-chemokine receptor 2 or a functional portion of said receptor, comprising contacting a composition comprising the receptor or portion with an effective amount of an

antibody or antigen-binding fragment thereof which binds to a mammalian CC-chemokine receptor 2 or portion of said receptor, wherein said antibody inhibits binding of said chemokine to mammalian CC-chemokine receptor 2 and inhibits one or more functions associated with binding of the ligand to the receptor.

31. A method according to Claim 30 wherein the chemokine is selected from the group consisting of MCP-1, MCP-2, MCP-3, MCP-4 and combinations thereof.

32. A method according to Claim 30 wherein the antibody or antigen-binding fragment is selected from the group consisting of:

a) monoclonal antibody 1D9;

b) an antibody having an epitopic specificity which is the same as or similar to that of 1D9;

c) an antibody which can compete with 1D9 for binding to mammalian CC-chemokine receptor 2; and

d) antigen-binding fragments of any of (a) through (c) which bind to mammalian CC-chemokine receptor 2 or a portion thereof.

33. A method of detecting or identifying an agent which binds a mammalian CC-chemokine receptor 2 or ligand-binding variant thereof, comprising combining

a) an agent to be tested;

b) an antibody or antigen-binding fragment selected from the group consisting of:

i) monoclonal antibody 1D9;

ii) an antibody having an epitopic specificity which is the same as or similar to that of 1D9;

iii) an antibody which can compete with 1D9 for binding to mammalian CC-chemokine receptor 2;

iv) monoclonal antibody 8G2;

v) an antibody having an epitopic specificity which is the same as or similar to that of 8G2;

vi) an antibody which can compete with 8G2 for binding to mammalian CC-chemokine receptor 2;

vii) antigen-binding fragments of any of (i) through (vi) which bind to mammalian CC-chemokine receptor 2 or a portion thereof; and

viii) combinations of the foregoing; and

c) a composition comprising a mammalian CC-chemokine receptor 2 or a ligand-binding variant thereof,

under conditions suitable for binding of said antibody or antigen-binding fragment to said mammalian CC-chemokine receptor 2 or ligand-binding variant thereof, and detecting or measuring binding of said antibody or antigen-binding fragment to said mammalian CC-chemokine receptor 2 or ligand-binding variant thereof.

34. A method according to Claim 33 wherein the formation of a complex between said antibody or antigen-binding fragment and said mammalian CC-chemokine receptor 2 or ligand-binding variant is monitored, and wherein a decrease in the amount of complex formed relative to a suitable control is indicative that the agent binds said receptor or ligand-binding variant thereof.

35. A method according to Claim 33 wherein the composition comprising a mammalian CC-chemokine receptor 2 or a ligand-binding variant thereof is a cell bearing recombinant CC-chemokine receptor 2 or ligand-binding variant thereof.

36. A method according to Claim 35, wherein the composition comprising a mammalian CC-chemokine receptor 2 or a ligand-binding variant thereof is a membrane fraction of said cell bearing recombinant CC-chemokine receptor 2 or ligand-binding variant thereof.

37. A method according to Claim 33 wherein the antibody or antigen-binding fragment thereof is labeled with a label selected from the group consisting of a radioisotope, spin label, antigen label, enzyme label, fluorescent group and chemiluminescent group.

38. A method according to Claim 33 wherein the agent is an antibody having specificity for a mammalian CC-chemokine receptor 2 or antigen-binding fragment thereof.

39. A method of inhibiting HIV infection in a patient, comprising administering to the patient a composition comprising an effective amount of an antibody or antigen-binding fragment thereof which binds to mammalian CC-chemokine receptor 2 or portion thereof and inhibits binding of HIV to the receptor or portion thereof.

40. A method according to Claim 39 wherein the antibody or antigen-binding fragment thereof is selected from the group consisting of:

a) monoclonal antibody 1D9;

b) an antibody having an epitopic specificity which is the same as or similar to that of;

c) an antibody which can compete with 1D9 for binding to mammalian CC-chemokine receptor 2; and

d) antigen-binding fragments of any of (a) through (c) which bind to mammalian CC-chemokine receptor 2 or a portion thereof.

41. A method of inhibiting leukocyte trafficking in a patient, comprising administering to the patient a composition comprising an effective amount of an antibody or antigen-binding fragment thereof which binds to a mammalian CC-chemokine receptor 2 or portion of said receptor and inhibits binding of a ligand to the receptor.

42. A method according to Claim 41 wherein the ligand is a chemokine.

43. A method according to Claim 42 wherein the chemokine is selected from the group consisting of MCP-1, MCP-2, MCP-3, MCP-4 and combinations of the foregoing.

44. A method according to Claim 41 wherein the antibody or antigen-binding fragment thereof is selected from the group consisting of:

a) monoclonal antibody 1D9;

b) an antibody having an epitopic specificity which is the same as or similar to that of 1D9;

c) an antibody which can compete with 1D9 for binding to mammalian CC-chemokine receptor 2; and

d) antigen-binding fragments of any of (a) through (c) which bind to mammalian CC-chemokine receptor 2 or a portion thereof.

45. A composition comprising an antibody or antigen-binding fragment thereof which binds to a mammalian CC-chemokine receptor 2 or portion of said receptor, wherein said antibody or antigen-binding fragment thereof inhibits binding of a ligand to the receptor, and an optional physiologically acceptable vehicle.

46. An antibody or antigen-binding fragment thereof which binds to a mammalian CC-chemokine receptor 2 or portion of said receptor, wherein said antibody or antigen-binding fragment thereof inhibits binding of a ligand to the receptor with an IC_{50} of less than about 1.0 μg/ml.

47. An antibody or antigen-binding fragment thereof according to Claim 46 wherein the IC_{50} is less than about 0.05 μg/ml.

48. An antibody or antigen-binding fragment thereof according to Claim 46 wherein the IC_{50} is less than about 0.05 μg/ml.

49. An antibody or antigen-binding fragment thereof which binds to a mammalian CC-chemokine receptor 2 or portion of said receptor, wherein said antibody or antigen-binding fragment thereof inhibits binding of a ligand to the receptor, and wherein the antibody or

antigen-binding fragment binds the receptor with an affinity of at least about 0.1×10^{-9} M.

50. An antibody or antigen-binding fragment thereof according to Claim 49, wherein the affinity is at least about 1×10^{-9} M.

51. An antibody or antigen-binding fragment thereof according to Claim 50, wherein the affinity is at least about 3×10^{-9} M.

52. A method of treating a CC-chemokine receptor 2-mediated disorder in a patient, comprising administering to the patient an effective amount of an antibody or antigen-binding fragment thereof which binds to mammalian CC-chemokine receptor 2 or portion thereof.

add B5

add B6

Add D1

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